

REMARKS

Upon entry of this Amendment, claims 1, 4-9, 23-25, 30, 32-40, 42, 44, 45, 47-51, 57, 59 and 61-64 will be pending. Claims 1, 4-6, 8, 9, 23-25, 32-40, 42, 44, 47, 49-51, 59, and 61-64, currently on file, have been amended to more clearly define the scope of protection being sought and to ensure consistent use of terms throughout. Claims 17-19, 31, 41 and 43, currently on file, have been canceled without prejudice or disclaimer. Claims 52-56 and 58, currently on file, have been withdrawn without prejudice or disclaimer.

The foregoing amendments are made without any intention to abandon the subject matter of the claims as filed, but with the intention that claims of the same, lesser, or greater scope may be pursued in a continuation, continuation-in-part, or one or more divisional applications. Applicant asserts that no new matter has been added by way of these amendments. The Examiner's bases for rejecting claims 1, 4, 5, 31, 33-41, 43, 52-56 and 58, currently on file, are addressed below.

Rejection of Claims under 35 U.S.C. § 112, First paragraph (Enablement)

The Examiner has maintained the rejection of claims 52-56 and 58, currently on file, under 35 U.S.C. §112, first paragraph, alleging that these claims lack enablement over the scope claimed, for the reasons of record set forth in the Office Actions mailed January 15, 2003, August 26, 2003 and August 5, 2004. The Examiner indicated that "Applicant's arguments filed 4-7-05 have been fully considered but they are not persuasive." Applicant assumes that the Examiner intended to refer to the Response filed on April 5, 2005 and has addressed the Examiner's remarks accordingly.

The Examiner has acknowledged in the Office Action that Applicant is enabled for a method of inhibiting human tumor growth *in vivo* (and inhibiting tumor cell growth *in vitro*) comprising the systemic administration of the antisense oligonucleotides of SEQ ID NOs: 1-3, 5,

6, and 8-12 (*e.g.* of 20-50 nucleobase lengths), and of antisense oligonucleotides of this size range that specifically target and inhibit human neuropilin of SEQ ID NO:33. The Examiner alleges, however, that Applicant is not enabled for a method of inhibiting the metastasis of melanomas *in vivo* comprising the administration of antisense oligonucleotides *in vivo*.

Applicant respectfully traverses this rejection and maintains for reasons set forth in the Responses filed on June 16, 2003, February 26, 2004, and April 5, 2005, that the specification is fully enabling for an *in vivo* method of inhibiting metastasis of human tumors, and in particular melanoma as recited in instant claims 52-56 and 58, using antisense oligonucleotides directed against a human neuropilin mRNA. Applicant reiterates that one skilled in the art would have a reasonable expectation that the *in vitro* and *in vivo* examples provided in the specification would correlate with the full scope of claims 52-56 and 58, currently on file, and asserts that one skilled in the art would be able to practice the instantly claimed invention without undue experimentation. In this regard, Applicant notes that in the previous Office Action mailed August 26, 2003, the Examiner had indicated that the instant disclosure is enabling for the inhibition of melanoma *in vivo* comprising administration of antisense oligonucleotides between 15-100 nucleobases in length which specifically target and inhibit the expression of SEQ ID NO:33, encoding human neuropilin.

Applicant, however, without conceding to the correctness of the Examiner's position, but in order to expedite prosecution of the instant application, has withdrawn claims 52-56 and 58, currently on file, without prejudice or disclaimer. Applicant reserves the right to prosecute the withdrawn subject matter in the present application or in a continuation, continuation-in-part, or one or more divisional applications. Applicant respectfully submits that withdrawal of claims 52-56 and 58, currently on file, renders the Examiner's rejection moot and, therefore, respectfully requests that this rejection be withdrawn.

Rejection of Claims under 35 U.S.C. § 103(a) (Obviousness)

The Examiner has rejected Claims 1, 4, 5, 31, 33-41 and 43, currently on file, as being unpatentable over He *et al.* and Soker *et al.* (hereinafter referred to as He and Soker, respectively), in view of Milner *et al.* and Baracchini *et al.* (hereinafter referred to as Milner and Baracchini, respectively). The Examiner has indicated that "Applicant's arguments filed 4-7-05 have been fully considered but they are not persuasive." With respect to the inherent property of the claimed antisense oligonucleotide to inhibit tumor growth, the Examiner further alleged that the claimed invention is drawn to compositions comprising antisense to neuropilin, but is not drawn to methods of inhibiting tumor growth and so, contrary to Applicant's assertions, the combined references render the instant invention obvious. As noted above, Applicant assumes that the Examiner intended to refer to the Response filed on April 5, 2005 and has addressed the Examiner's remarks accordingly.

Applicant respectfully traverses this rejection and maintains for reasons set forth in the Responses filed February 26, 2004, and April 5, 2005, that nothing in the cited prior art teaches or even suggests the instantly claimed antisense oligonucleotides which inhibit neuropilin expression and tumor cell growth in a human, or pharmaceutical compositions and vectors comprising same.

For example, Applicant reasserts that there is nothing in He or Soker that suggests a link between the new VEGF receptor identified in Soker, which at the time of the article, had yet to be purified and characterized, and the neuropilin receptor for the Sema-III protein described in He. As discussed previously, He teaches a human neuropilin in the context only of elucidating *in vitro* the mechanisms and pathway by which the Sema-III protein mediates its effects on axons. Nothing in He suggests that neuropilin is in any way related to the VEGF receptor identified by Soker, nor does anything in He suggest that neuropilin is a suitable target for cancer therapies. As such, one skilled in the art would not have been motivated to apply Milner to design antisense oligonucleotides directed against neuropilin mRNA having the sequence of SEQ ID NO:33, or to prepare pharmaceutical compounds or vectors comprising such antisense oligonucleotides.

Finally, there is nothing in Baracchini that cures the fundamental defects of He, Soker or Milner taken alone or in combination. Accordingly, Applicant maintains that one of ordinary skill in the art would not have been motivated to combine the teachings of He with Soker along with Milner or Baracchini to address the problems that are solved by the instant application relating to the design and application of antisense oligonucleotides against neuropilin, nor would the skilled worker, having regard to the teachings in these references, have any expectation of being able to successfully produce antisense oligonucleotides, pharmaceutical compositions or vectors having the claimed properties.

Applicant, however, without conceding to the correctness of the Examiner's position, but in order to expedite prosecution of the instant application, has amended independent claims 1, 4 and 5, currently on file, to recite "[a]n antisense oligonucleotide from about 20 to 100 nucleotides in length" that "comprises a sequence selected from the group consisting of SEQ ID NOs:1, 2, 3, 5, 6, 8, 9, 10, 11 and 12". Applicant reserves the right to prosecute any subject matter canceled from the claims currently on file in a continuation, continuation-in-part, or divisional application.

Applicant asserts that He, Soker, Milner and Baracchini alone or in combination do not teach or suggest all the claim limitations of amended independent claims 1, 4 and 5. Applicant submits that amended claims 1, 4 and 5, and claims dependent thereon meet the requirements of 35 U.S.C. § 103(a) and, therefore, respectfully requests that the Examiner withdraw this rejection.

ALLOWABLE SUBJECT MATTER

Applicant acknowledges, with thanks, the Examiner's comments that SEQ ID NOs: 1-3, 5, 6 and 8-12 are free of the prior art searched and of record, and also that claims 6-9, 17-19, 23-35, 30, 32, 42-44, 45, 47-51, 57, 59 and 61 appear free of the prior art searched and of record.

In re Application of:
Wright et al.
Application No.: 09/296,264
Filed: April 22, 1999

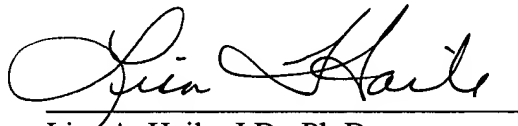
PATENT
Attorney Docket No.: MBM1250-2

CONCLUSION

On the basis of the foregoing claim amendments and remarks, Applicant respectfully submits that, upon entry, the pending claims will be in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

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Lisa A. Haile, J.D., Ph.D.
Registration No. 38,347
Telephone: (858) 677-1456
Facsimile: (858) 677-1465

DLA PIPER RUDNICK GRAY CARY US LLP
4365 Executive Drive, Suite 1100
San Diego, CA 92121-2133
USPTO Customer Number 28213